IRELL & MANELLA LLP
David I. Gindler (117824) (dgindler@irell.com)
Andrei Iancu (184973) (aiancu@irell.com)
Amir Naini (226627) (anaini@irell.com)
1800 Avenue of the Stars, Suite 900
Los Angeles, California 90067-4276
Telephone: (310) 277-1010
Facsimile: (310) 203-7199

Attorneys for Plaintiff and Counterclaim Defendant
Ariosa Diagnostics, Inc.

UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF CALIFORNIA

SAN FRANCISCO DIVISION

ARIA DIAGNOSTICS, INC.,

Plaintiff,

vs.

SEQUENOM, INC.,

Defendant.

SEQUENOM, INC.,

Counterclaim Plaintiff,

vs.

ARIA DIAGNOSTICS, INC.,

Counterclaim Defendant,

and

ISIS INNOVATION LIMITED,

Nominal Counterclaim Defendant.

Case No. 3:11-cv-06391-SI

ARIOSA'S OPPOSITION TO SEQUENOM'S MOTION FOR PRELIMINARY INJUNCTION

Date of Hearing: June 15, 2012
Time of Hearing: 9:00 a.m.
Location: Courtroom 10
19th Floor

Judge: Hon. Susan Illston

REDACTED PUBLIC VERSION

TABLE OF CONTENTS

Page

TABLE OF AUTHORITIES

Page(s)

Cases

Page(s)

Statutes

Rules

I. INTRODUCTION

Ariosa Diagnostics, Inc. (formerly, Aria Diagnostics) is a startup company that commenced operations in mid-2010 to develop an innovative non-invasive prenatal test. The result of Ariosa's research and development is the Harmony Prenatal Test, which Ariosa brought to market in March 2012. The Harmony test employs a novel and proprietary way of analyzing cell-free DNA in maternal blood to determine whether a fetus is at risk of having an extra copy of certain chromosomes (referred to as a trisomy), such as chromosome 21 ("trisomy 21," which causes Down syndrome). The Harmony test is entirely different than what is claimed in the '540 patent—and shutting it down would destroy Ariosa as a company and deprive pregnant women of an innovative, accurate, and affordable medical test.

Sequenom's preliminary injunction motion completely ignores a critical threshold issue: The '540 patent does not cover patentable subject matter. The patent itself states that it "has now been discovered that foetal DNA is detectable in maternal serum or plasma samples." Bischoff Decl. Ex. 2 at 1:50-51. But this is an unpatentable natural phenomenon. As the Supreme Court recently reiterated in *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, 132 S. Ct. 1289 (2012), Section 101 of the Patent Act bars issuance of a patent on the "discovery" of a natural law or phenomenon. Moreover, that natural phenomenon does not become patentable where, as here, it has simply been combined with additional steps consisting "of well understood, routine, conventional activity already engaged in by the scientific community." *Id.* at 1298. The '540 patent does no more than combine conventional techniques, such as "amplifying" and "detecting" certain fetal DNA, with the "discovery" that this DNA naturally exists in maternal blood. To allow the '540 patent to stand would stifle innovation—such as Ariosa's development of the Harmony test—that makes use of this natural phenomenon.

Even if this threshold issue were ignored, Sequenom would fare no better in its efforts to show infringement of the '540 patent. During prosecution, the PTO required the applicants to limit all claims to the detection of "*paternally inherited* nucleic acid," which the specification describes (and the PTO understood) as a sequence "*not possessed by the mother*." Bischoff Decl. Ex. 2 at 2:58-59 (emphasis added). The claims are thus confined to the detection of fetal nucleic

acid inherited from the father *and exclude the detection of fetal nucleic acid inherited from the mother*. The Harmony test is fundamentally different than this claim scope. The Harmony test does not identify nucleic acid of fetal origin by reference to a sequence known to be possessed by the father and absent from the mother. Rather, the Harmony test processes *all* cell-free copies of certain chromosomes in a maternal blood sample, without regard to whether they are fetal and inherited from the mother, fetal and inherited from the father, or from the mother herself.

Sequenom's misguided effort to stretch its claims to cover Ariosa's test flies in the face of the prosecution history. During prosecution of the '540 patent, the applicants sought to broadly cover the detection of *any* "nucleic acid of foetal origin," whether inherited from the father or the mother. The PTO repeatedly rejected those claims—and required the applicants to limit all claims to the detection of "paternally inherited nucleic acid"—because the specification did not enable any method of detecting a nucleic acid of fetal origin other than by reference to a sequence known to be possessed by the father and absent from the mother. Sequenom's argument that the claims cover *any* method of detecting a paternally inherited nucleic acid, irrespective of whether that nucleic acid is known to be possessed by the father and absent from the mother, would read this PTO-imposed limitation right out of the claims.

Moreover, after failing to obtain this broad claim scope in the '540 patent, the applicants tried again in a continuation application, in which they pursued claims that were broadly drawn to the detection of nucleic acid of fetal origin "which differs" from "that of the maternal genome." The applicants were candid about their reasons for seeking this claim scope: They desired to cover detection of Down syndrome, *which they acknowledged was a* ***maternally inherited condition*** *that would fall outside the "paternally inherited" limitation of the '540 patent*. The PTO repeatedly rejected those claims too, explaining that "the specification does not describe or discus[s] 'detecting the presence of a fetal nucleic acid which differs from that of the maternal genome.'" *Id.* Ex. 31 at 2. The applicants ultimately abandoned the continuation application and all further efforts to secure broader claims. Yet Sequenom now accuses Ariosa of infringement despite admitting that the Harmony test does exactly what the PTO rejected and the applicants abandoned: it looks for "the presence of a fetal nucleic acid which differs from that of the

maternal genome." *Id.* Ex. 52 at 123:12-17. It is black-letter law that Sequenom cannot try to recapture in this litigation what the applicants sought and abandoned after repeated PTO rejections during prosecution.

The '540 patent would have other serious problems if broadly construed, as Sequenom would like, to cover a non-invasive test for Down syndrome. Sequenom offers no explanation for why it took fourteen years after the '540 patent's 1997 priority date to develop a non-invasive test for Down syndrome, despite the "long-held goal" of doing so. Mot. at 4. The explanation is simple: The '540 patent claims are not enabled if they are broadly construed to encompass non-invasive tests for trisomies. It is this very lack of enablement that caused the PTO to repeatedly reject the applicants' efforts to secure broad claims, including claims that the applicants drafted for the specific purpose of covering a non-invasive test for Down syndrome. Indeed, Dr. Dennis Lo (a '540 patent inventor) has recently conceded that "prior to 2007," *ten years after the priority date*, "most experts working in this area [thought] that this technology cannot be used for the prenatal diagnosis of Down syndrome," and that such tests have been made possible only "over the last two or three years, with the development of next generation DNA sequencing . . . ." Fearon Decl. Ex. 13 at 1-2.

The long dry spell after 1997 was not for lack of trying. Sequenom omits any mention of its own spectacular (and highly publicized) failure to develop a non-invasive test for Down syndrome. That history is highly informative for enablement, because the pressure created by trying to practice the '540 patent without any meaningful guidance from the specification was apparently so great that Sequenom resorted to criminal fraud in 2008 and 2009 by reporting falsified data about SEQureDx, its earlier non-invasive test for Down syndrome, to convince investors and the market that it had finally developed a test that practiced its patent. An SEC investigation and cease-and-desist order ensued—resulting in a guilty plea from a top Sequenom scientist and the abandonment of SEQureDx as a scientific fraud.

Sequenom's broad reading of the '540 patent claims results in invalidity for still another reason: All of the claims would be anticipated by an article published in 1995 by Kazakov *et al*., entitled "Extracellular DNA in the Blood of Pregnant Women." If the claims were construed to

encompass amplifying and detecting paternally inherited nucleic acids irrespective of whether they are identified as paternally inherited—and irrespective of whether fetal nucleic acids inherited from the mother and nucleic acids of the mother herself are also amplified and detected—then all claims necessarily would be invalid in light of the Kazakov reference.

Sequenom cannot make any other showing required to secure a preliminary injunction. Sequenom's claims of irreparable harm are inherently (and fatally) flawed because they *intentionally ignore* the presence of Verinata Health, another competitor in the market offering its own non-invasive test for Down syndrome. Sequenom makes no effort whatsoever to distinguish any impact of Verinata (or anyone else in the market) from competition by Ariosa. This defect infects multiple aspects of Sequenom's arguments because no alleged price erosion, lost sales, or lost market share—which Sequenom has failed to show in any event—can be attributed to Ariosa rather than another competitor such as Verinata. Finally, the balance of equities and the public interest strongly favor Ariosa. A preliminary injunction, if granted, would remove Ariosa's only product from the market and effectively destroy Ariosa as a business. Investors would lose their money and employees would lose their jobs. And the public would be harmed, too: It would lose the benefit of a superior non-invasive medical test that Ariosa has made available to all pregnant women, not just those falling in the "high-risk" category for whom Sequenom can charge a higher price. Sequenom's motion should be denied.

II. ARGUMENT

"[A] preliminary injunction is an extraordinary and drastic remedy, one that should not be granted unless the movant, *by a clear showing*, carries the burden of persuasion." *Mazurek v. Armstrong*, 520 U.S. 968, 972 (1997) (internal quotation marks omitted). To secure a preliminary injunction, Sequenom must establish that it "is likely to succeed on the merits, that [it] is likely to suffer irreparable harm in the absence of preliminary relief, that the balance of equities tips in [its] favor, and that an injunction is in the public interest." *AstraZeneca LP v. Apotex, Inc.*, 633 F.3d 1042, 1049 (Fed. Cir. 2010) (internal quotation marks omitted). Sequenom has failed to make a "clear showing" on any of these elements.

A. Sequenom is Not Likely to Succeed on the Merits

Sequenom alleges that Ariosa infringes independent claims 1, 24, and 25 and dependent claims 2, 8, and 19-22 of the '540 patent. Sequenom sets forth claim 1 as representative of the asserted claims. Claim 1 recites:

> A method for detecting a paternally inherited nucleic acid of fetal origin performed on a maternal serum or plasma sample from a pregnant female, which method comprises
>
> amplifying a paternally inherited nucleic acid from the serum or plasma sample and
>
> detecting the presence of a paternally inherited nucleic acid of fetal origin in the sample.

"A preliminary injunction should not issue if an alleged infringer raises a *substantial question regarding either infringement or validity, i.e.*, the alleged infringer asserts an infringement or invalidity defense that the patentee has not shown lacks substantial merit." *Id.* at 1050 (emphasis added).[1] As discussed below, Ariosa has raised numerous "substantial questions" regarding the merits of Sequenom's patent-infringement claims.

1. The Asserted Claims are Not Drawn to Patentable Subject Matter

Sequenom's motion should be denied because the presence of cell-free fetal DNA in maternal plasma or serum is a natural phenomenon, not patentable subject matter. It is a fundamental and long-standing principle of patent law that no one can patent discoveries of natural laws or phenomena. 35 U.S.C. § 101. They are the basic tools of scientific and technological work and are "part of the storehouse of knowledge of all men . . . free to all men and reserved exclusively to none." *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 130 (1948).

In *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, 132 S. Ct. 1289 (2012), the Supreme Court cautioned against the problems that result from attempts to claim unpatentable

[1] Contrary to Sequenom's suggestion, Mot. at 7, "the alleged infringer at the preliminary injunction stage does not need to prove invalidity by the 'clear and convincing' standard that will be imposed at trial on the merits." *Titan Tire Corp. v. Case New Holland, Inc.*, 566 F.3d 1372, 1379 (Fed. Cir. 2009). "[I]f the trial court concludes there is a 'substantial question' concerning the validity of the patent, meaning that the alleged infringer has presented an invalidity defense that the patentee has not shown lacks substantial merit, it necessarily follows that the patentee has not succeeded in showing it is likely to succeed at trial on the merits of the validity issue." *Id.*

subject matter, noting that it "has repeatedly emphasized . . . a concern that patent law not inhibit further discovery by improperly tying up the future use of laws of nature." *Id*. at 1301. The *Mayo* decision reaffirmed and crystalized earlier admonitions that clever draftsmanship cannot be used to circumvent Section 101. The Supreme Court stated that a natural phenomenon is not made patentable by claiming "additional steps [that] consist of well understood, routine, conventional activity already engaged in by the scientific community; and those steps, when viewed as a whole, add nothing significant beyond the sum of their parts taken separately." *Id.* at 1298.

All of the asserted claims are directed to paternally inherited nucleic acid of fetal origin in a maternal serum or plasma sample. There is no dispute that the presence of these paternally inherited nucleic acids in serum or plasma is a natural phenomenon experienced by pregnant women. Fearon Decl. ¶ 69, Ex. 9 at 167:14-25. The discovery of a natural phenomenon is not itself a patentable invention. *Gottschalk v. Benson*, 409 U.S. 63, 67 (1972) ("Phenomena of nature, though just discovered, mental processes, and abstract intellectual concepts are not patentable, as they are the basic tools of scientific and technological work.").

All of the asserted claims recite additional steps that offer nothing beyond conventional techniques applied to a natural phenomenon. For example, claim 1 adds the steps of "amplifying" and "detecting" nucleic acid from a maternal serum or plasma sample. Dr. Tatman, Sequenom's Vice President of Business Development, admitted at his deposition that the invention is "[t]he general ability to detect and analyze extracellular fetal nucleic acids in maternal circulation," and that the applicants "discovered the presence of such fetal nucleic acids in maternal circulation and the ability to detect those *using standard technologies* of the time." Naini Decl. Ex. 1 at 35:5-36:5. Sequenom's expert Dr. Evans also admitted these facts at his deposition. Fearon Decl. Ex. 9 at 188:5-17 ("Q: Others before Dr. Lo amplified and detected nucleic acids, right? A: Yes. Q: In fact, traditional DNA diagnostics well before 1997 traditionally involved three steps, right: Sample preparation, amplification, and detection, correct? A: Commonly. Q: And the others before Dr. Lo amplified and detected nucleic acid in plasma and serum, true? A: Yes.").

Nothing in the '540 patent itself suggests that the "additional steps" of amplifying and detecting nucleic acids of fetal origin in serum or plasma involve anything beyond "well

understood, routine, conventional activity already engaged in by the scientific community" at the time. To the contrary, the specification itself acknowledges that amplification of fetal DNA sequences can be done using "standard" systems. *Id.* Ex. 2 at 2:43-45 ("An amplification of foetal DNA sequences in the sample is normally carried out. Standard nucleic acid amplification systems can be used . . . ."). The same is true with respect to the detection of nucleic acids in a serum or plasma sample. The specification acknowledges, for example, that others had "demonstrated that tumour DNA can be detected by the polymerase chain reaction (PCR) in the plasma or serum . . . ." *Id.* 1:40-42. Ariosa respectfully refers the Court to the expert declaration of Dr. Eric Fearon for a detailed analysis of each asserted claim under Section 101. *Id.* ¶¶ 52-121.

2. Ariosa Does Not Infringe the '540 Patent Because the Harmony Test Does Not Meet the "Paternally Inherited Nucleic Acid" Limitation Found in Every Asserted Claim

Even if the claims of the '540 patent were drawn to patentable subject matter, Ariosa would have no liability because it does not infringe any of these claims. All of the claims are limited to amplifying and detecting "paternally inherited nucleic acid." The correct construction of "paternally inherited nucleic acid" is: "known sequence received only from the father, and not fetal sequence which differs from that of the mother." As discussed below (and described in detail in the expert declaration of Farideh Bischoff at ¶¶ 102-20), the Harmony test does not meet this limitation because it does not detect sequence known to be received only from the father; it detects nucleic acid with *no regard* for whether it was received from the father.

a. "Paternally Inherited Nucleic Acid" Means a Known Sequence Received Only from the Father and Not Fetal Sequence Which Differs from That of the Mother

The phrase "paternally inherited nucleic acid" is a critical claim limitation. The applicants were required to add this limitation during prosecution of the '540 patent to confine the scope of the claims to what was actually disclosed and enabled in the specification. The specification and prosecution history of the '540 patent—as well as the abandonment of broad claims in a continuation application intended to cover the detection of Down syndrome and other trisomies—demonstrate that Ariosa offers the correct interpretation of this limitation.

(1) Ariosa's Claim Construction is Derived from the Language of the Specification and Supported by the Applicants' Experimental Results

"[T]he best source for understanding a technical term is the specification from which it arose, informed, as needed, by the prosecution history." *Phillips v. AWH Corp*., 415 F.3d 1303, 1315 (Fed. Cir. 2005) (internal quotation marks omitted). Ariosa's construction of "paternally inherited nucleic acid" is based on, and grounded in, the specification of the '540 patent.

In the section entitled "Summary and Objects of the Invention," the specification states: "The method *according to the invention* can be applied to the detection of any *paternally-inherited sequences which are not possessed by the mother* . . . ." Bischoff Decl. Ex. 2 at 2:57-59 (emphasis added). This statement sets forth the critical concept—completely ignored by Sequenom—that "paternally inherited" sequences "are not possessed by the mother." This language confines the scope of the claimed invention to detecting known sequences *received **only** from the father*; "not possessed by the mother" excludes any method that detects sequences received from the mother. *See Verizon Servs. Corp. v. Vonage Holdings Corp.*, 503 F.3d 1295, 1308 (Fed. Cir. 2007) (referring to language in the Disclosure of the Invention section of the specification, "[w]hen a patent thus describes the features of the 'present invention' as a whole, this description limits the scope of the invention").

All of the experimental results in the specification support this conclusion—and make clear that sequence to be detected must be one that is *known* to be received from the father. The specification does not disclose or enable any method of determining whether a nucleic acid is of fetal origin other than by reference to a sequence that is *known* to be received from the father and absent from the mother. Four of the five experiments involve detecting fetal gene sequences that are known to reside on the Y chromosome. Bischoff Decl. ¶¶ 50-55. Because the Y chromosome is known to be absent from a woman's genome, these experiments necessarily involve detecting a known sequence received only from the father. The other experiment involves detecting a particular fetal blood group gene—the Rhesus-D ("RhD") gene—in "RhD-negative" mothers, who are known to lack the RhD gene. *Id.* ¶ 53. Because the RhD gene is known to be absent from those mothers' genomes, the experiment necessarily involves detecting a known sequence

received only from the father. *Id.*

Other passages of the specification also support this conclusion. For example, in a description of how to detect "mutations" in "[p]aternally-inherited DNA," the specification states that the method "require[s] the prior genotyping of the father and mother [*i.e.*, determining the genetic sequence of the mother and father at a particular location on a chromosome] and then an allele for detection [*i.e.*, a sequence variation between the mother and father at that location] will be chosen which is present in the father, but is absent in the mother." *Id.* Ex. 2 at 3:20-24. The specification provides a similar explanation when describing detection of a "beta-globin gene," a gene that naturally has many different mutations in the general population. The specification states: "Provided that the father and mother carry different mutations [in their beta-globin sequences], the paternal mutation [inherited by the fetus] can be used as an amplification target . . . ." *Id.* at 3:6-8. As Dr. Bischoff explains, targeting the paternally inherited mutation for amplification requires knowledge of the paternal sequence prior to performing the test. *Id.* ¶ 48.

Sequenom would have the Court interpret "paternally inherited nucleic acid" in the broadest conceivable sense: a nucleic acid that "is inherited from the father." Mot. at 8. This interpretation ignores the applicants' own description of what it means to detect a paternally inherited nucleic acid: "the detection of any paternally-inherited sequences *which are not possessed by the mother*." Bischoff Decl. Ex. 2 at 2:58-59 (emphasis added). Sequenom's approach is contrary to well-established canons of claim construction and should be rejected.

(2) Ariosa's Claim Construction is Supported by the Prosecution History of the '540 Patent

Sequenom ignores not only the specification of the '540 patent, but also its prosecution history. The PTO required the applicants to include this limitation because (as demonstrated above) the specification discloses only one method of detecting fetal nucleic acid in maternal plasma: detection of a known sequence received only from the father.

The applicants tried at the outset to secure claims *without any limitations* on the fetal nucleic acids subject to detection (*i.e.*, "detecting the presence of a nucleic acid of foetal origin in the sample"). *Id.* Ex. 4 at 39. The PTO rejected this broad scope "because the specification . . .

does not reasonably provide enablement for . . . detecting fetal nucleic acid in general . . . ." *Id.* Ex. 10 at 5. The PTO observed that the specification only enables "detecting the presence of paternally inherited fetal DNA . . . wherein the fetal DNA is from the Y chromosome and for detecting the presence of the RhD gene in maternal plasma from an RhD negative pregnant wom[a]n," *id.*—the five experiments described in the specification. Thus, the PTO found enablement *only* where the sequence to be detected is known to be received from the father.

The PTO never wavered from this position. When the applicants persisted in seeking the same broad claims, the PTO repeated the same rejection in a final office action—this time, with specific reference to the applicants' statement that their invention is applicable "'to the detection of any paternally-inherited sequences *which are not possessed by the mother*.'" *Id.* Ex. 12 at 11 (emphasis added). Indeed, the PTO explained that "detection of a maternally inherited nucleic acid would be unpredictable and require undue experimentation." *Id.* The applicants responded to the final office action by agreeing to add the "paternally inherited" limitation now found in all claims of the '540 patent. In remarks accompanying the amendment, the applicants noted that, during a telephone interview, "the Examiner advised that the claims would be allowable if limited to 'paternally inherited' nucleic acid, since the specification is enabling for detecting paternally inherited nucleic acid in maternal serum or plasma." *Id.* Ex. 13 at 3.

Sequenom cannot be allowed to erase this critical limitation. Doing so would permit Sequenom to recapture through claim construction what the applicants gave up to obtain allowance during prosecution. *See, e.g., Chimie v. PPG Indus. Inc.*, 402 F.3d 1371, 1384 (Fed. Cir. 2005) ("The purpose of consulting the prosecution history in construing a claim is to exclude any interpretation that was disclaimed during prosecution. . . . Such a use of the prosecution history ensures that claims are not construed one way in order to obtain their allowance and in a different way against accused infringers.") (citations and internal quotation marks omitted).

Sequenom's proposed construction—any nucleic acid "inherited from the father"—would have the intended effect of eliminating any relevance to the PTO-imposed limitation. This is because a fetus inherits half of its DNA from the mother and the other half from the father (along with various mutations). Under Sequenom's construction, a test that *randomly* detects fetal

nucleic acids in maternal plasma would, by implication, meet this limitation, even when absolutely nothing is known about the source of any nucleic acid of fetal origin actually detected. That construction cannot be squared with the prosecution history.

(3) Ariosa's Claim Construction is Supported by the Prosecution History of the Continuation Application

Ariosa's construction of the phrase "paternally inherited nucleic acid" includes an important negative limitation at the end: "known sequence received only from the father, *and not fetal sequence which differs from that of the mother*." This negative limitation is required by the PTO's repeated rejection of, and the applicants' decision to abandon their quest for, broad claims in a continuation directed to a method of detecting nucleic acid of fetal origin "which differs" from that of the mother. Bischoff Decl. ¶¶ 59-67. The PTO rejected these claims because the specification does not provide support for a method of detecting differences between fetal sequences and maternal sequences. The negative limitation ensures that the '540 patent conforms to the PTO's rejection of this broader claim scope.[2]

A representative claim from this continuation application reads as follows: "A detection method performed on a maternal serum or plasma sample from a pregnant female, which method comprises *detecting the presence of a fetal nucleic acid in the sample by detecting nucleic acid which differs qualitatively or quantitatively from that of the maternal genome*." *Id.* Ex. 27 at 1-2 (emphasis added). The applicants were explicit about their reasons for pursuing claims that, unlike those in the '540 patent, were not limited to detecting "paternally inherited nucleic acid": They wanted to cover detection of Down syndrome, but recognized that the "additional chromosome 21 present in a Down's affected fetus . . . is usually derived from the egg and is thus maternally inherited." *Id.* at 14. The applicants urged that, because of the limitation to "paternally inherited nucleic acid," the '540 patent claims covered "just one specific example" of their invention. *Id.* at 7. Dr. Lo added in a sworn declaration that "[i]t is not necessary for the success

[2] *See Microsoft Corp. v. Multi-Tech Sys., Inc.*, 357 F.3d 1340, 1350 (Fed. Cir. 2004) ("Any statement of the patentee in the prosecution of a related application as to the scope of the invention would be relevant to claim construction . . . .").

of the method of the present invention that the gene to be detected be paternally inherited" and that the "invention can be used to diagnose Down's syndrome in a fetus . . . ." *Id.* Ex. 28 at 9.

The PTO repeatedly rejected these claims. The PTO noted that the continuation application "broadened the claims from paternally inherited, which was patented, to detecting the presence of a fetal nucleic acid which differs from that of the maternal genome . . . ." *Id.* Ex. 31 at 3. The PTO explained, however, that the specification's "description *does not support detecting the presence of a fetal nucleic acid which differs from that of the maternal genome*." *Id.* (emphasis added). In maintaining the claim rejections in subsequent exchanges, the PTO stated that "*the instant specification does not appear to be directed to . . . differences between maternal and fetal DNA,*" and that "[t]he disclosure of paternally inherited nucleic acids in the instant specification does not mean that the specification also supports maternally inherited." *Id.* Ex. 39 at 6, 10 (emphasis added). After a final office action rejecting every proposed claim, the applicants abandoned the application and all efforts to secure additional claims. *Id.* ¶ 67.

Sequenom will likely point out that the specification suggests that the "method according to the invention can be applied to screening for Down's Syndrome . . . ." *Id.* Ex. 2 at 3:26-27. The applicants relied on this very same language during prosecution of the continuation application, *id.* Ex. 27 at 14, and the PTO repeatedly found that it did not support claims to a method of detecting fetal sequence "which differs" from maternal sequence, *id.* ¶¶ 64-66. The PTO explained (and Ariosa's expert Dr. Fearon agrees, Fearon Decl. ¶¶ 141-45) that none of the experimental results reported in the specification provides a method of actually implementing this suggestion. Bischoff Decl. Ex. 47 at 2-3. This language, which the PTO found inadequate to support claims that the applicants drafted to cover a test for Down syndrome, cannot be used by Sequenom to expand the scope of the '540 patent claims to cover exactly what the applicants were unable to secure in the continuation application.

The negative limitation—"and not fetal sequence which differs from that of the mother"—is thus necessary to give effect to the applicants' unambiguous statements in the continuation prosecution history that "paternally inherited nucleic acid" cannot be equated with (or interpreted to encompass) fetal sequence which differs from that of the maternal genome. *See N. Am.*

Container, Inc. v. Plastipak Packaging, Inc., 415 F.3d 1335, 1343-45 (Fed. Cir. 2005) (construing "generally convex" to require "a majority of convex points along the inner wall *and no concave points*" because of arguments during prosecution distinguishing inner wall with concavity) (emphasis added). The applicants expressly contrasted the scope of the allowed claims in the '540 patent with the scope of the desired claims in the continuation application. The PTO understood the very different claim scope that the applicants sought—and repeatedly told the applicants that the specification did not support it. The applicants' decision to abandon these broader claims precludes Sequenom from trying to construe the '540 patent to capture this abandoned subject matter. *See Schriber-Schroth Co. v. Cleveland Trust Co.*, 311 U.S. 211, 218 (1940) ("Where the patentee in the course of his application in the patent office has, by amendment, cancelled or surrendered claims, those which are allowed are to be read in the light of those abandoned and an abandoned claim cannot be revived and restored to the patent by reading it by construction into the claims which are allowed.").

The negative limitation is also consistent with, and supported by, the specification and the prosecution history of the '540 patent itself. The specifications of the '540 patent and its continuation are identical. As the PTO repeatedly told the applicants during prosecution of the continuation, the specification "does not support detecting the presence of a fetal nucleic acid which differs from that of the maternal genome." Bischoff Decl. Ex. 31 at 3. It is for this very reason that the PTO required the applicants during prosecution of the '540 patent to limit all claims to the detection of "paternally inherited nucleic acid"—the only method disclosed in the patent of detecting a nucleic acid of fetal origin. The negative limitation thus ensures that the '540 patent claims have the scope—and only the scope—that the PTO intended to permit and that the applicants agreed to accept.

b. Ariosa's Harmony Test Does Not Detect Known Sequence Received Only from the Father, and Not Fetal Sequence Which Differs from That of the Mother

The Harmony test involves the simultaneous use of two novel and sophisticated DNA sequencing assays—the "non-polymorphic" assay and the "polymorphic" assay—that together determine the risk that a maternal plasma sample contains an abnormally elevated number of

chromosome 13, 18 or 21 of fetal origin. (An assay in this context is a test or analysis of DNA. *Id.* ¶ 76.) Neither assay infringes any asserted claim of the '540 patent because neither is limited to detecting "paternally inherited nucleic acid" (which, as stated above, means known sequence received only from the father, and not fetal sequence which differs from that of the mother).

The non-polymorphic assay of the Harmony test targets specific locations (referred to as "loci") on chromosomes 13, 18 and 21 that typically do not vary in a population, *i.e.*, all individuals are expected to have the same sequence at these loci. *Id.* ¶ 118. The non-polymorphic assay counts the number of times that these loci are identified in a maternal plasma sample to determine the proportions of chromosomes 13, 18 and 21 in the sample. *Id.* The assay counts *all* copies of chromosomes 13, 18 and 21 by examining these loci *with no regard to their origin*. The assay does not identify (or in any way discriminate between) nucleic acids of fetal origin or nucleic acids of the mother herself. Nor does the assay identify (or in any way discriminate between) chromosomes inherited from the father or chromosomes inherited from the mother. Accordingly, this assay does not detect nucleic acid of fetal origin by reference to any sequence that is known to be possessed by the father and absent from the mother. Instead, it indiscriminately counts all sequences at specific loci irrespective of whether they are sequences of fetal origin inherited from the father, sequences of fetal origin inherited from the mother, or sequences of the mother herself. For these reasons, this assay does not infringe any asserted claim.

Sequenom's expert Dr. Evans agrees that the non-polymorphic assay never distinguishes between maternal and fetal nucleic acid, or maternally inherited and paternally inherited nucleic acid. Evans Decl. ¶ 108. Instead, he contends that detecting a paternally inherited nucleic acid does not require distinguishing it from other nucleic acids in the sample. *Id.* According to Dr. Evans, the non-polymorphic assay detects at least some paternally inherited nucleic acid of fetal origin that, by implication, must be included in the undifferentiated mass of nucleic acids that are subject to the assay. *Id.* As discussed above, that interpretation reads the "paternally inherited" limitation right out of the claims because it renders the claim scope no different than detecting fetal nucleic acid in general. The applicants tried, and failed, to secure claims during

prosecution of the '540 patent to detecting any "nucleic acid of fetal origin." As Dr. Evans agrees, that is what the non-polymorphic assay does: "Q. And it's detecting the presence of all nucleic acid of fetal origin in the sample? A. Yes." Bischoff Decl. Ex. 52 at 199:10-12.

The polymorphic assay of the Harmony test determines the overall proportion of fetal nucleic acid relative to maternal nucleic acid in a maternal plasma sample (called the "fetal fraction") by examining sequences at loci on chromosomes 1 through 12 where "fetal alleles differ from maternal alleles." *Id.* ¶¶ 83-84. An "allele" in this context is a sequence variation at the selected loci. *Id.* ¶ 84. By examining chromosomal loci where different sequences are expected to occur in the mother and the fetus, the polymorphic assay determines the percentage of fetal nucleic acids and the percentage of maternal nucleic acids in the sample. The fetal fraction information is used in combination with the non-polymorphic assay to create a statistical computation of trisomy risk. *Id.* ¶¶ 89-91. This assay does not detect nucleic acid of fetal origin by reference to any sequence that is known to be possessed by the father and absent from the mother. It uses an entirely different method—one predicated on knowing chromosomal locations where maternal and fetal sequences will differ (but without knowing anything about the actual genome of the father or mother). For these reasons, this assay does not infringe any asserted claim of the '540 patent.

The polymorphic assay does not infringe for another important reason: It does *exactly* what Drs. Lo and Wainscoat tried, without success, to claim in their continuation application. The polymorphic assay *detects the presence of fetal nucleic acid in the sample which differs from that of the maternal genome.* Dr. Evans agrees with this description of the polymorphic assay. Evans Decl. ¶ 111. The PTO repeatedly rejected the applicants' efforts to secure this exact claim scope in the continuation application because the specification "*does not support detecting the presence of a fetal nucleic acid which differs from that of the maternal genome*." Bischoff Decl. Ex. 31 at 3 (emphasis added). Ariosa and the public have a right to rely on this indelible public record.

Dr. Evans takes the position that, by detecting fetal nucleic acid that differs from maternal nucleic acid, the polymorphic assay is "by implication" detecting what "*must come* from the father." *Id.* Ex. 52 at 123:16-17 (emphasis added). This argument, which would treat the scope of "paternally inherited nucleic acid" as essentially equivalent to the scope of "fetal nucleic acid

which differs from that of the maternal genome," is foreclosed by the prosecution history of the continuation application. The applicants explained that the latter is different from, and broader than, the former—and the PTO denied this different and broader claim scope. The applicants sought that different and broader claim scope so that they could capture non-invasive tests for Down syndrome. They failed. Ariosa cannot be found to infringe precisely what the PTO said that specification does not disclose or enable and what the applicants ultimately abandoned.

c. The Harmony Test Does Not Meet the "Amplifying" Limitation

All claims of the '540 patent require "amplifying" a paternally inherited nucleic acid. The correct construction of "amplifying" a paternally inherited nucleic acid is: "increasing the relative concentration of" paternally inherited nucleic acid.

This construction is supported by the specification, which refers to enrichment methods as being *specific* for particular sequences. *Id.* Ex. 2 at 2:39-42 ("A sequence-based enrichment method could also be used on the maternal serum or plasma to specifically enrich for foetal nucleic acid sequences."). Consistent with this description, all experimental results in the specification involve use of an amplification method called polymerase chain reaction to target known sequences received only from the father—and no others. *Id.* ¶ 127. Because those paternally inherited sequences are specifically and exclusively targeted in the examples, their amplification increases their relative concentration compared to other nucleic acids. *Id.* This makes sense: Because the patent is focused on ultimately detecting a fetal nucleic acid inherited from the father, the method needs to increase the relative concentration of that particular nucleic acid to make it easier to detect from among all other nucleic acids in the sample. *Id.* Ex. 12 at 10.

Extrinsic evidence also supports Ariosa's construction. Sequenom's expert Dr. Evans testified that amplifying a nucleic acid means enriching it. *Id.* ¶ 124. Dr. Evans also agrees that enrichment in the context of nucleic acids means "increasing the concentration of" one nucleic acid "relative to" another. *Id.* ¶ 125. Moreover, in the context of nucleic acids and genetics, Stedman's Medical Dictionary's definition for "amplification" refers to "increasing the proportion" of one nucleic acid to that of another. *Id.* ¶ 126. In sum, all relevant evidence supports construing "amplifying" to mean "increasing the relative concentration of."

The Harmony test does not meet the "amplifying" limitation because it does not increase the *relative* concentration of paternally inherited nucleic acid compared to any other nucleic acid. *Id.* ¶ 128. As discussed above, Ariosa's test targets loci on chromosomes inherited from both the mother and the father. All of the sequences at those loci—those inherited from the mother and those inherited from the father—are amplified. Because Harmony does not target and amplify known sequence received only from the father, it does not increase the relative concentration of paternally inherited nucleic acid. *Id.*

Sequenom does not dispute these facts about Ariosa's test. Rather, Sequenom argues that *any increase* in the amount of paternally inherited nucleic acid, even when increased along with fetal nucleic acids inherited from the mother and nucleic acids of the mother herself, satisfies the "amplifying" limitation. Mot. at 9. Once again, this argument reads the "paternally inherited" limitation right out of the claim. There is a fundamental difference, which cannot be ignored, between the patent claims and the Harmony test: In the patent, paternally inherited nucleic acids are targeted for amplification to enable their detection; in the Harmony test, nucleic acids are amplified with no regard for their parental origin—because the Harmony test has no need to increase the copy number of paternally inherited nucleic acid as compared to any other nucleic acid in the sample. Accordingly, the Harmony test does not meet the "amplifying" paternally inherited nucleic acid limitation.

d. The Asserted Claims are Not Enabled

Enablement requires that "one skilled in the art, after reading the specification, could practice the claimed invention without undue experimentation." *AK Steel Corp. v. Sollac*, 344 F.3d 1234, 1244 (Fed. Cir. 2003). "The scope of the claims must be less than or equal to the scope of the enablement to ensure that the public knowledge is enriched by the patent specification to a degree at least commensurate with the scope of the claims." *Sitrick v. Dreamworks, LLC*, 516 F.3d 993, 999 (Fed. Cir. 2008) (internal quotation marks omitted). If Sequenom's claim constructions are correct (and they are not) and the asserted claims of the '540 patent cover a method of detecting Down syndrome, then the asserted claims of the '540 patent encompass subject matter far beyond the teaching of the specification and the state of the art in 1997. One

skilled in the art could not have practiced the asserted claims in 1997 to detect Down syndrome (or any other trisomy) on cell-free nucleic acids without undue experimentation. This is precisely why the PTO repeatedly rejected the applicants' many efforts to secure broader claims.

No sequencing technologies from 1997 were accurate enough to differentiate a maternal plasma sample having two fetal copies of chromosome 21 (or any other chromosome) from a plasma sample having three fetal copies of that chromosome. Fearon Decl. ¶ 142. It would take over a decade for development of the "next generation" sequencing technologies that are incorporated into the non-invasive prenatal tests now coming onto the market for the first time. *Id.* Attempts to develop a non-invasive test of cell-free nucleic acids for Down syndrome before the availability of these "next generation" sequencing technologies met with sustained failure. *Id.* ¶¶ 137-40. Sequenom itself failed with respect to an earlier non-invasive test for Down syndrome called SEQureDx—and then tried to hide that failure by reporting falsified data, resulting in an SEC investigation, a guilty plea to criminal fraud by a senior Sequenom scientist, and the firing of Sequenom executives and scientists. Naini Decl. Exs. 2, 3. Moreover, just last year, Dr. Lo admitted that, "prior to 2007, most experts working in this area [thought] that this technology cannot be used for the prenatal diagnosis of Down syndrome and it has actually taken us 10 years to solve this problem," and that this was made possible only "over the last two or three years, with the development of next generation DNA sequencing . . . ." Fearon Decl. Ex. 13 at 1-2. Dr. Lo has confirmed in a recent scientific publication his view that next generation technologies were necessary to enable a non-invasive prenatal test for Down syndrome using cell-free nucleic acid in maternal plasma. *Id.* Ex. 12.

Sequenom argues that the '540 patent specification includes references to "quantitative" methods that are sufficient to enable its broad reading of the claims. The PTO found those references to be unpersuasive, as it repeatedly rejected for lack of enablement the applicants' efforts to secure claims broad enough to cover detection of Down syndrome. Bischoff Decl. ¶¶ 63-67. The PTO was correct: The passages in the specification that Sequenom identifies merely sketch out rudimentary methods that did not teach a person of skill in 1997 how to make a working quantitative test for the detection of Down syndrome through the use of cell-free nucleic

acids in maternal plasma. Fearon Decl. ¶¶ 141-45.

The '540 patent specification enables no more than the detection of paternally inherited nucleic acids—known sequence received only from the father. That is what the PTO concluded when requiring the inclusion of this limitation in all claims of the '540 patent, and when rejecting the applicants' efforts to secure broader claims (and, in particular, claims that the applicants intended to cover the detection of Down syndrome, a genetic disorder ordinarily inherited from the mother). If Sequenom's broad construction of the '540 patent claims were correct—and it is not—then the asserted claims would not be enabled.

e. The Asserted Claims are Anticipated by Kazakov

Finally, the '540 patent was not the first to disclose the methods of the asserted claims if, as Sequenom suggests, the claims are broad enough to cover any method which amplifies and detects a paternally inherited nucleic acid, irrespective of whether the method is able to discriminate, identify, or isolate which nucleic acids are paternally inherited. A claim is invalid by anticipation if every limitation of the claim is expressly or inherently disclosed in a single prior art reference. *Atlas Powder Co. v. IRECO Inc.*, 190 F.3d 1342, 1347 (Fed. Cir. 1999). "Under the principles of inherency, if the prior art necessarily functions in accordance with, or includes, the claimed limitations, it anticipates," regardless of whether those of ordinary skill in the art would have recognized the inherent characteristics. *Id*.

In 1995, Kazakov *et al*. published an article entitled "Extracellular DNA in the Blood of Pregnant Women," which details, at least two years before applicants' patent application, tests on cell-free DNA found in the blood of pregnant women. Fearon Decl. Ex. 4 at 232 ("The level of extracellular DNA increases in the blood of women during pregnancy."). Kazakov and his colleagues stated that the extracellular (*i.e.*, cell-free) DNA that they detected "may" include fetal DNA. *See id.* at 235 ("[C]ells of the fetus . . . and the mother . . . may excrete DNA."). Although Sequenom might try to argue that the use of the word "may" suggests that Kazakov was not certain as to the origin of the cell-free DNA, this argument would make no difference: The doctrine of "inherent anticipation" applies regardless of whether a skilled artisan at the time would have been certain that the extracellular DNA included fetal DNA.

The Kazakov reference meets every limitation of the asserted claims as interpreted by Sequenom. The method of representative claim 1 has two steps. First, it requires "amplifying a paternally inherited nucleic acid from the serum or plasma sample" of a pregnant woman. Kazakov and his colleagues first prepared serum samples from the blood of pregnant women. *Id.* ¶ 152. They then amplified extracellular nucleic acid sequences known as "Alu repeats" from these serum samples using polymerase chain reaction (the same amplification technique used in the patent). *Id.* Alu repeats are present on all human chromosomes and are thus present on every chromosome in the fetal genome (including the Y chromosome), whether inherited from the father or the mother. *Id.* ¶ 158. By amplifying cell-free Alu repeats of nucleic acid from the serum of pregnant women—which we know included cell-free fetal nucleic acid—Kazakov necessarily amplified a paternally inherited nucleic acid of fetal origin in the serum sample (under Sequenom's claim construction). *Id.* The Kazokov reference thus meets the amplification step if "amplifying" means (as Sequenom contends) increasing the absolute copy number of the target sequence, irrespective of any increase in the copy number of any other nucleic acid.

Second, claim 1 requires "detecting the presence of a paternally inherited nucleic acid of fetal origin in the sample." Kazakov and his colleagues detected the amplified Alu repeats, which necessarily included the paternally inherited Alu repeats of fetal origin, using a conventional method called gel electrophoresis. *Id*. Ex. 4 at 232 ("[T]he full-size Alu repeats were observed among extracellular blood DNA repeats of pregnant women. . . . [T]he PCR method allowed to observe in the blood DNA fragments flanked by inverted Alu repeats (inter Alu repeats). The presence of such a type of inter Alu repeats was estimated . . . .").

Thus, every limitation of claim 1, as interpreted by Sequenom, is anticipated by the Kazakov reference. A similar analysis applies to every other asserted claim, and Ariosa respectfully directs the Court's attention to Dr. Fearon's expert declaration for a claim-by-claim analysis showing that the Kazakov reference renders the '540 patent invalid. *Id*. ¶¶ 146-68.

B. Sequenom Has Not Demonstrated Irreparable Harm

To obtain a preliminary injunction, Sequenom must prove irreparable harm likely will occur absent an injunction. *See Amazon.com, Inc. v. Barnesandnoble.com, Inc.*, 239 F.3d 1343,

1350 (Fed. Cir. 2001). After the Supreme Court's decision in *eBay Inc. v. MercExchange, L.L.C.*, 547 U.S. 388 (2006), irreparable harm cannot be presumed. *Robert Bosch LLC v. Pylon Mfg. Corp.*, 659 F.3d 1142, 1149 (Fed. Cir. 2011). Rather, the plaintiff must demonstrate a specific nexus between the alleged infringement and harm that cannot be compensated by monetary damages. *Hologic, Inc. v. Senorx, Inc.*, 2008 WL 1860035, at *17 (N.D. Cal. Apr. 25, 2008) (irreparable harm not shown where any pricing pressure or market share loss could be compensated by monetary damages; speculative evidence of harm insufficient).

1. Sequenom Has Not Shown Irreparable Price Erosion

There is no evidence that Sequenom is experiencing "drastic" and "irreversible" price erosion—or any price erosion at all. Sequenom just recently announced a contract with Multiplan, a major managed health care network, [redacted]

Even if Sequenom's prices were to decline in the future, there is no evidence that any lower prices would be *attributable to Ariosa*.[4] Sequenom's expert Dr. Rao acknowledged that even if Ariosa were enjoined, numerous sources of downward pressure on Sequenom's prices would exist, including "potentially anybody else who is competing in the same marketplace with a noninvasive test to detect fetal abnormalities, along with other economically substitutable

[3] The absence of any evidence showing that Sequenom has been negatively impacted by Ariosa's January product announcement and March product launch is particularly notable because Sequenom's economic expert, Dr. Rao, testified that he expected any harm to commence immediately. Sullivan Decl. ¶ 65, Ex. 14 at 34:8-35:9.

[4] *Travel Tags, Inc. v. UV Color, Inc.*, 690 F. Supp. 2d 785, 800 (D. Minn. 2010) (rejecting irreparable harm where patentee's declaration "assumes, without providing support, that [defendant's] prices were solely responsible for [patentee's] price erosion"); *Belden Techs. Inc. v. Superior Essex Commc'ns LP*, 802 F. Supp. 2d 555, 577 (D. Del. 2011) ("Plaintiffs' argument of price erosion due to the presence of defendants' infringing product is also unpersuasive as the industry experienced an overall decrease in market price . . . .").

products, including amnio and CVS." Sullivan Decl. Ex. 14 at 81:1-8. Sequenom ignores these factors, instead basing its price erosion argument on the false premise that Ariosa is its only competitor. In fact, Verinata is offering a test nearly identical to Sequenom's with prices ranging from $300 to $1,200 per test. *Id.* ¶ 51, Ex. 17. Dr. Rao testified that Sequenom had not asked him to analyze, and he had no opinion on, "whether there is any incremental impact of Ariosa above and beyond what's already occurring with Verinata." *Id.* Ex. 14 at 200:18-201:10. By contrast, Ariosa's expert Dr. Sullivan analyzes the full scope of economic factors influencing Sequenom's pricing and explains that Ariosa's presence in the market has little, if any, additional effect on Sequenom's prices. *Id.* ¶¶ 47-54.

2. Sequenom Has Not Shown Irreparable Market Share Loss

Sequenom's arguments regarding lost sales are similarly deficient. As in the case of price erosion, there is simply no evidence of lost sales. Sequenom has been thriving since Ariosa's January product announcement and March product launch. Sales for Sequenom have been so strong that, on April 16 (almost three months after Ariosa's product announcement), Sequenom issued a press release notifying investors that it was revising upward its internal goal of 2012 sales, from 25,000 to 40,000 tests. *Id.* ¶ 64. Sequenom cites no cases finding irreparable harm where the patentee increased its sales after an accused infringer entered the market.[5]

Sequenom provides no facts about its market share, other than to note that its "stated goal is to sell 25,000 MaterniT21 tests in 2012," Mot. at 18—a goal which, as noted above, Sequenom now has revised upwards. Sequenom provides no economic analysis showing that Ariosa will reduce that share. Dr. Rao disavowed any such opinion at his deposition. Sullivan Decl. Ex. 14 at 20:21-24 ("Q. When you signed the declaration, had you attempted to quantify the degree to which Sequenom would experience lost sales, if any? A. No."). Moreover, Sequenom's Chief Executive Officer testified at deposition that he is "not aware of *any* sales that have actually been lost by Sequenom to Ariosa." *Id.* Ex. 11 at 30:20-23 (emphasis added). As discussed in detail by

[5] Indeed, Sequenom's expert does not opine that any harm to Sequenom in this category would be irreparable. At deposition, he testified that lost sales "typically are quantifiable," and that "the two aspects of [his] opinion that relate to harm that could theoretically be irreparable is the price erosion and the inability to raise capital." Sullivan Decl. Ex. 14 at 40:9-19.

Dr. Sullivan, there is no reason that Ariosa's entry into this large, available market should cause Sequenom's sales to decline. [redacted] Finally, Sequenom again fails to allocate any of the alleged harm to Ariosa, as opposed to Verinata and other market factors.

For all of these reasons, Sequenom has not demonstrated an irreparable loss of market share. *See, e.g.*, *Nutrition 21 v. United States*, 930 F.2d 867, 871 (Fed. Cir. 1991) ("[N]either the difficulty of calculating losses in market share, nor speculation that such losses might occur, amount to proof of special circumstances justifying the extraordinary relief of an injunction prior to trial."); *Presidio Components Inc. v. Am. Tech. Ceramics Corp.*, 723 F. Supp. 2d 1284, 1336 (S.D. Cal. 2010) (finding no irreparable harm where the market included multiple competitors and products); *Advanced Cardiovascular Sys., Inc. v. Medtronic Vascular, Inc.*, 579 F. Supp. 2d 554, 559-60 (D. Del. 2008) (rejecting irreparable harm where alleged infringer gained relative to both competitors in the market, not just patentee).

3. Sequenom Has Demonstrated No Loss of Ability to Raise Capital

Sequenom's contention that Ariosa's presence in the market will prevent Sequenom from raising sufficient capital also is contradicted by the facts. At deposition, Dr. Tatman, Sequenom's Vice President of Business Development, testified that, during his twelve years at Sequenom, it has *never* had any difficulty raising capital. Sullivan Decl. Ex. 8 at 162:2-7; 147:23-148:1; Ex. 14 at 48:22-49:1. Moreover, on January 25, 2012, after Ariosa announced its product launch, Sequenom raised $62 million in capital in a fully-subscribed financing round. *Id.* ¶ 70. There is

[redacted]

simply no indication that investors are abandoning Sequenom because of Ariosa; to the contrary, Sequenom's share price has been trending upwards since Ariosa's launch of the Harmony test. *Id.* ¶¶ 64-70; *see also id.* Ex. 14 at 56:24-57:24 (no analyst downgrades because of Ariosa).

4. Sequenom Has Not Shown Loss of Goodwill

There is no evidence to show that an injunction is necessary to prevent loss of "goodwill." Sequenom's first argument, that absent an injunction, it "would be deprived from marketing to physicians that Sequenom is the exclusive purveyor of a noninvasive test that uses Sequenom's patent-protected technology" fails at the outset because Ariosa and Sequenom are not the only competitors in the field. Sequenom's second argument, that "if Aria puts an inferior service on the market, or if it markets its service 'off-label' . . . Aria will poison the market," is also baseless. Sequenom identifies no deficiency in Ariosa's test, nor any facts to suggest that a deficiency in Ariosa's product would negatively impact Sequenom's reputation. Stuelpnagel Decl. ¶¶ 20-34; Bischoff Decl. ¶¶ 136-41.

5. Sequenom Has Not Demonstrated Ariosa Cannot Satisfy a Judgment

Sequenom's suggestion that Ariosa will not be able to satisfy a judgment should be rejected. Sequenom's own economic expert disclaimed any such opinion at his deposition. Sullivan Decl. Ex. 14 at 131:1-6 ("Q. Do you believe that Ariosa would be unable to satisfy an award of damages were Sequenom to prevail in this lawsuit? A. Well, as I discuss in my declaration, I do not have any information on Ariosa's financial position to be able to make that determination."). Sequenom provides no estimate of its anticipated damages, much less any analysis of Ariosa's ability to pay them. Sequenom does not contend that Ariosa is inadequately capitalized or that Ariosa's business model is deficient in any respect. Sequenom cites no authority, and there is none, for its suggestion that a defendant's status as a venture-capital funded operation supports injunctive relief.

C. The Balance of Hardships Weighs Decidedly in Ariosa's Favor

The balance of hardships is not a close call. Sequenom is thriving despite Ariosa's presence in the market. In contrast, granting an injunction would irreparably damage Ariosa. The Harmony test is its only product; enjoining Ariosa pending resolution of this litigation would

destroy it as a business. Stuelpnagel Decl. ¶ 35; Sullivan Decl. ¶¶ 79-83. Sequenom, citing *permanent* injunction case law, argues that Ariosa "has no basis to complain that it would lose sales if it were enjoined." Mot. at 23-24. But this law does not apply when, as here, there has been no adjudication of infringement. In the *preliminary* injunction context, where the balance of hardships is a crucial factor, Ariosa has every right to complain—and the Court must consider—that an injunction would put Ariosa out of business before any finding of liability. *Bell & Howell Document Mgmt. Prods. Co. v. Altek Sys.*, 132 F.3d 701, 708 (Fed. Cir. 1997) (prospect of putting defendant out of business if a preliminary injunction issued "is a proper factor to be considered").

D. The Requested Injunction is Detrimental to the Public Interest

Sequenom identifies no public interest served by depriving consumers of another choice in health care services, beyond "protection of patent rights." This "interest" exists in every patent case—and it exists to a far lesser extent here because Sequenom expended no time or expense developing the claimed invention but instead in-licensed the '540 patent years after it issued. These facts contrast starkly with *Sanofi-Synthelabo v. Apotex, Inc.*, 470 F.3d 1368 (Fed. Cir. 2006), where the patentee spent $800 million to develop the patented technology. *Id*. at 1383.

All other public interest considerations weigh against injunctive relief. A preliminary injunction would deprive patients of access to an important new medical procedure. Unlike Sequenom, which makes its test available to (and serves only a fraction of) the worldwide market of "high risk" patients, Ariosa does not prevent physicians from ordering Harmony for patients falling outside the "higher risk" category—because its cost structure permits it to price the test low enough to be accessible to a broader segment of the population. In short, the public has much to lose, and nothing to gain, from the granting of a preliminary injunction against Ariosa.[7]

III. CONCLUSION

Sequenom has failed to make a "clear showing" that it has satisfied any or all of the required elements to secure a preliminary injunction. Its motion should be denied.

[7] If a preliminary injunction were to be granted, the undertaking required pursuant to Federal Rule 65(c) would be, at a minimum, Ariosa's valuation because Ariosa likely could not recover from being shut down pending trial. Ariosa stands ready at the Court's request to submit documentation thereof.

Dated: May 15, 2012

Respectfully submitted,

IRELL & MANELLA LLP
David I. Gindler
Andrei Iancu
Amir Naini

By: */s/ David I. Gindler*

David I. Gindler
Attorneys for Plaintiff and Counterclaim Defendant
Ariosa Diagnostics, Inc.